Optimizing renal replacement therapy in older adults: a framework for making individualized decisions

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It is often difficult to synthesize information about the risks and benefits of recommended management strategies in older patients with end-stage renal disease since they may have more comorbidity and lower life expectancy than patients described in clinical trials or practice guidelines. In this review, we outline a framework for individualizing end-stage renal disease management decisions in older patients. The framework considers three factors: life expectancy, the risks and benefits of competing treatment strategies, and patient preferences. We illustrate the use of this framework by applying it to three key end-stage renal disease decisions in older patients with varying life expectancy: choice of dialysis modality, choice of vascular access for hemodialysis, and referral for kidney transplantation. In several instances, this approach might provide support for treatment decisions that directly contradict available practice guidelines, illustrating circumstances when strict application of guidelines may be inappropriate for certain patients. By combining quantitative estimates of benefits and harms with qualitative assessments of patient preferences, clinicians may be better able to tailor treatment recommendations to individual older patients, thereby improving the overall quality of end-stage renal disease care.

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There is substantial variation in the type and intensity of care provided to older patients with end-stage renal disease (ESRD),[1] stemming from uncertainty about the benefits and harms of ESRD treatment strategies in this growing population. Many older patients starting dialysis have multiple chronic conditions in addition to ESRD.[2] As comorbidity accumulates, average life expectancy, functional status, and quality of life decline. However, there is considerable heterogeneity in both life expectancy and treatment preferences among older patients. This heterogeneity makes it difficult to synthesize information about the risks and benefits of recommended interventions for individual patients.

Clinical practice guidelines for ESRD care have traditionally taken an age-neutral approach, allowing clinicians flexibility to adapt guidelines to individual patients, but providing little guidance about how to do this. Quality improvement initiatives in ESRD care advocate for quality benchmarks, but often fail to identify patients who may not benefit from the standard of care. Some have noted that both guidelines and quality initiatives do not acknowledge the trade-offs involved in managing patients with multiple chronic conditions, or the value that patients place on achieving these outcomes.[3]

For example, although it may be intuitive that older patients on average derive less benefit than their younger counterparts from interventions like kidney transplantation, some older patients may derive substantial benefit, whereas others will not benefit at all and may even be harmed. For interventions such as hypertension treatment, older adults have a higher absolute risk of cardiovascular events but also a higher risk of adverse events from treatment. Reconciling these competing factors to make treatment decisions is often complex and the resulting uncertainty can lead to both under- and overtreatment of older adults.

Clinicians must also prioritize these treatment decisions (e.g., by prioritizing the kidney transplant evaluation, there may be less time for home dialysis training). Integrating treatment preferences with considerations of risks and benefits is central to individualized decision-making because it allows patients to prioritize the outcomes that matter to them.

We propose a conceptual framework to guide management decisions for older patients with ESRD. Our framework is adapted from a framework proposed for cancer screening in the elderly that considers three factors: life expectancy, the benefits and harms of competing treatment strategies, and the patient's preferences.[4] We apply this framework to three aspects of decision-making for older patients with (or expected to develop) ESRD: selection of a dialysis modality, choice of vascular access for hemodialysis (HD), and referral for kidney transplantation. Using available data, we provide quantitative estimates to compare treatment strategies in older patients with different life expectancies. Although there are several established methods for quantifying an intervention's benefits or risks,[5] we use the number needed to treat (NNT), the reciprocal of the absolute risk reduction. There is no one value for the NNT that defines a beneficial intervention; however the closer to 1 the NNT then the larger the benefit. Details of the data sources and the computational methods are provided in the Supplementary Information online. Using this framework, we illustrate how clinicians could more effectively tailor treatment strategies to individual ESRD patients by combining quantitative estimates of benefits and harms with qualitative assessments of patient preferences.

LIFE EXPECTANCY AFTER DIALYSIS INITIATION AMONG OLDER PATIENTS

Life expectancy after the start of dialysis for the 25th, 50th and 75th percentile of patients aged 65 and older in the United States is presented in Figure 1. Median life expectancy declines with age, from 2.5 years for 65–69 year olds, to 0.6 years for patients $\geqslant$90 years. Among patients of similar ages, there is considerable heterogeneity, including among the very elderly. For example, life expectancy of an 80-year-old patient with ESRD at the 75th percentile (3.0 years) is more similar to the life expectancy of a 70-year-old patient also at the 75th percentile (4.3 years) than it is to the life expectancy of an 80-year-old patient at the 25th percentile (0.4 years).

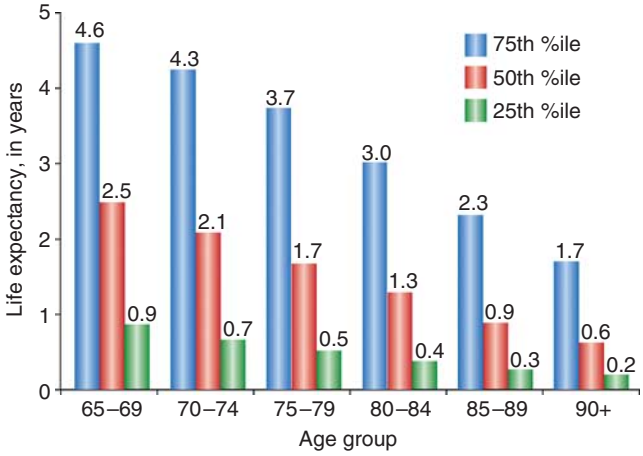

Figure 1 | Quartiles of life expectancy after dialysis initiation by age group.

Clinical characteristics may help clinicians estimate a patient's life expectancy after dialysis initiation. For example, Moss *et al.*[6] described the utility of the surprise question ('Would I be surprised if this patient died in the next year?') for predicting short-term mortality. Validated prognostic models may also be used to estimate life expectancy among dialysis patients.[7–10] Most focus on short-term mortality risk,[8,9] although some are also useful for predicting long-term mortality risk.[10] Several are simple enough to adapt to practice.[8,10] Perfectly accurate predictions of life expectancy are not necessary to use this framework. Rather, reasonable estimates of whether a patient is above or below the median life expectancy for his or her age will allow clinicians to make better assessments of the risks and benefits of various management strategies.

DIALYSIS MODALITY SELECTION

Population-level risks and benefits of peritoneal dialysis vs. hemodialysis

Among patients over the age of 65 with ESRD in the United States, in-center HD is the initial modality for 93–98% of patients, peritoneal dialysis (PD) is the initial modality for 2-5% of patients, preemptive kidney transplant for 0–2% of patients, and home HD for $<$1% (Figure 2). Our discussion of modality selection focuses on comparisons of in-center HD vs. PD, as outcomes data for home HD, particularly in the elderly, are limited. For the same reasons, we also consider various PD modalities together.

Recent observational studies suggest that survival of incident PD patients in the US has improved over time, and is now comparable to survival of incident HD patients.[11,12]

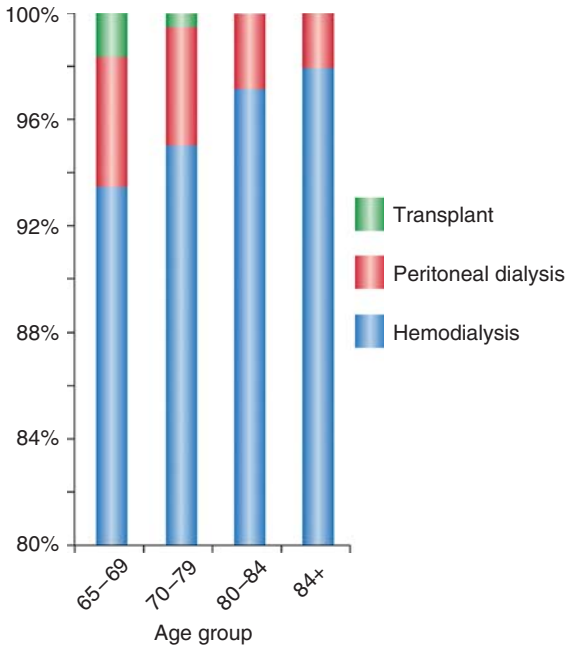

Figure 2 | Initial renal replacement therapy modality in the United States in 2008, according to age group.

Table 1 | Number needed to treat with PD to prevent one hospitalization for sepsis due to hemodialysis with a CVC

	65–69 years			70–74 years			75–79 years			80–84 years			85–89 years			⩾90 years		
	Quartiles of life expectancy																	
Treatment strategy	75th	50th	25th	75th	50th	25th	75th	50th	25th	75th	50th	25th	75th	50th	25th	75th	50th	25th
PD vs. CVC Model 1	3	6	17	3	5	17	3	7	22	5	11	37	4	11	39	6	16	51
PD vs. CVC Model 2	5	9	25	4	8	24	4	10	33	7	17	58	7	18	62	11	31	99

Abbreviations: CVC, central venous catheters; HD, hemodialysis; PD, peritoneal dialysis.
Model 1: Assumes patients remain on modality for their remaining lifetime.
Model 2: Incorporates age-specific modality switch rates (Supplementary Information online) and assumes that patients who switch from PD to HD do so with a CVC.

A notable exception is the subgroup of diabetic patients ⩾65 years of age with comorbidity. In this subgroup survival with PD has improved over time but remains lower than for HD.[11,12] Paradoxically the improvement in PD survival for most patient subgroups has occurred as PD utilization has declined, perhaps pointing to unmeasured selection bias.

If survival is comparable or nearly comparable with PD and HD, what other modality-related outcomes matter? A variety of outcomes have been considered in the literature, including modality transfer, peritonitis, sepsis, access procedures, quality of life and satisfaction with care.[13–15] Modality transfer occurs more commonly with PD vs. HD, and is most often attributable to medical causes—recurrent peritonitis, ultrafiltration failure, and catheter malfunction.[13] Modality transfer is associated with greater treatment burden, higher costs of care and possibly greater morbidity;[16] thus it may be an outcome that clinicians and patients would like to avoid. Although in some countries older patients have similar or lower rates of transfer from PD to HD as compared with younger patients,[14] in the US older patients are more likely to transfer from PD to HD, and less likely to transfer from HD to PD as compared with younger patients (Supplementary Information online). In contrast to modality transfers, serious infection related morbidity occurs more commonly among HD patients, particularly those dialyzed through central venous catheters (CVCs). Serious infection rates for both modalities decline slightly between the ages of 65–85, and then increase over the age of 85 for patients on HD.[17] The competing effects of infectious morbidity and modality transfer may explain the observation that early mortality is lower for PD vs. HD, whereas late mortality is higher.[18] That is, PD confers an early benefit from avoiding infectious morbidity associated with a CVC, but a higher late risk due to the high rate of modality failure and transfer to HD with a CVC.[19]

Risks and benefits of dialysis modalities in patients with differing life expectancies

To assess the relative importance of these events in patients with different life expectancies, we estimated the NNT with PD vs. HD with a CVC to prevent one sepsis hospitalization. We first calculated the remaining lifetime risk of sepsis hospitalization for each modality. We then estimated the absolute risk reduction associated with PD, allowing us to calculate the NNT. Next, we compared this to the NNT after incorporating the age-specific modality transfer rates (Supplementary Information online), assuming that patients who switch from PD to HD do so with a CVC.

This analysis shows that PD confers a substantial advantage in reducing rates of hospitalization for sepsis as compared with HD with a CVC among many older patients (Table 1). For example, the NNT with PD to prevent one sepsis hospitalization is six or less for older adults above the 75th percentile of life expectancy for their age group. In other words, we would have to treat six older patients with these characteristics with PD to prevent one sepsis hospitalization due to HD with a CVC. The advantage of PD over HD with a CVC diminishes after accounting for modality transfer. For example, among patients aged 80–84 years with an average life expectancy, the NNT increases from 11 to 17 after accounting for modality transfer. For those in the lowest quartile of life expectancy, the NNTs increase above 25. This suggests that PD would confer a lower lifetime risk of hospitalization for sepsis compared with HD with a CVC in older adults with average or above average life expectancy. However, in older adults with poor life expectancy on dialysis, there is not a strong rationale for choosing PD over HD with a CVC in order to reduce sepsis risk. Similarly, in older patients with above average life expectancy on dialysis, risk of sepsis does not provide a strong rationale for choosing PD over HD with an arteriovenous fistula (AVF) or graft (AVG) (NNTs >25 for all age groups favoring AVF or AVG over PD). If the rate of CVC-related sepsis is significantly higher at some centers compared with national averages, or if a substantial percentage of patients who transfer from PD to HD are able to avoid CVCs, then PD would be more favorable than the estimates presented in Table 1.

With respect to patient-reported outcomes, changes in quality of life over time are similar among PD vs. HD patients, although PD patients report greater satisfaction with care.[15,20] PD patients require fewer access procedures than patients receiving HD with a CVC.[21] PD also preserves residual renal function to a greater extent than HD. This may allow older patients to maintain an attenuated PD regimen with relatively low treatment burden for an extended period of time. Conversely, because of higher protein losses, PD may contribute to a higher incidence of malnutrition.

VASCULAR ACCESS

Population-level risks and benefits of vascular access options for hemodialysis

Guidelines recommend the use of a permanent access (vs. CVC) for chronic dialysis, and strongly favor AVFs over AVGs.[22] These recommendations are based on the lower risk of infection and thrombosis associated with AVF vs. AVG use, and the high risk of infection associated with CVC use. Higher rates of hospitalization and mortality have also been reported for patients with AVGs compared with AVFs, and CVCs compared with AVGs, although it is unclear to what extent these results reflect confounding by unmeasured differences between patients with these different forms of access.[22] Compared with AVGs, AVFs have higher patency rates and require fewer procedures to maintain patency.[22] However, they have the disadvantage of requiring a substantial amount of time to mature and require more procedures to achieve patency compared with AVGs. Many AVFs ultimately fail to mature and time to maturation can be extraordinarily difficult to predict in an individual patient.[22] Older patients are generally more likely than their younger counterparts to experience failed maturation.[23,24] Although AVGs require more secondary procedures than AVFs to maintain patency, they can usually be used with reasonable certainty within weeks of creation. CVCs have the unique advantage that they can be placed at very short notice and can be used immediately after placement. As the time between access placement and first use is typically much longer for AVFs than for AVGs, the decision to place an AVF in preference to an AVG in a patient already receiving dialysis usually implies longer time spent with a CVC. In the US, approximately 80% of patients initiate chronic HD with a CVC, either because a permanent access had not been placed or because permanent access is not ready for use.[25]

The relative advantages and disadvantages of these different forms of access have been well documented on a population level. However, because the benefits and harms associated with each form of access accrue at different rates over time,[26,27] the net benefit of different access strategies might vary between individuals as a function of life expectancy. Although a variety of different outcomes including patency, infection, mortality, and hospitalization are more favorable for patients with an AVF compared with other forms of access, these benefits do not accrue immediately. For example, it is estimated that AVG survival is actually superior to that of AVFs for the first 18 months after creation, suggesting that patients with a life expectancy of less than this do not experience the benefit of longer patency expected after AVF placement.[28] Patients whose life expectancy is less than the 3–6 months required for maturation cannot benefit from AVF placement. For patients in whom maturation is expected to take longer than average or those at high risk of maturation failure, a life expectancy longer than six months would be needed to justify AVF placement. Given the higher risk of bacteremia and other adverse outcomes associated with CVC vs. AVG use, the need for prolonged CVC use during AVF maturation may be considered a harm if the patient will not live long enough to reap the benefits of AVF vs. AVG placement.

The relative advantages and disadvantages of each form of access may also vary depending on the timing of access placement relative to dialysis initiation. Although most patients undergo permanent access placement only after dialysis initiation, guidelines recommend that permanent access be placed in advance of the need for dialysis.[22] Compared with access decisions for patients already on dialysis, pre-dialysis access decisions involve an expanded and more complex set of considerations. Not only is the time required for AVF maturation unpredictable in individual patients, the time available before dialysis initiation is usually not known. There may also be uncertainty about whether the patient will survive long enough to require dialysis.[29,30] Patients may be uncertain about whether they would want dialysis, should the need arise.[31] Patients who do not survive to the point of needing dialysis, or decide not to undergo dialysis cannot benefit from access placement.[30] One recent study found that two-thirds of elderly decedents who had undergone AVF placement died before their AVF was ever used for dialysis, either because they did not start dialysis or because their AVF did not reach maturity.[32]

Risks and benefits of vascular access strategies in patients with differing life expectancies

To better understand the complex interplay between life expectancy and the relative advantages and disadvantages of these three distinct, but interdependent forms of HD access, we estimated the remaining lifetime absolute risk reduction in vascular access–related bacteremia attributable to the use of a preferred vs. non-preferred form of access (i.e., AVF vs. AVG and AVG vs. CVC, respectively) for patients with differing life expectancy. We defined an access-related bloodstream infection as a patient with a microorganism identified in a blood culture where the source of infection was the vascular access site.[33] We used this information to estimate the number of AVFs needed to prevent one episode of AVG-related bacteremia and the number of AVGs needed to prevent one episode of CVC-related bacteremia, respectively. We first assumed that permanent access was functional at the time of dialysis initiation. We then assumed that permanent access was placed at the time of dialysis initiation and that patients dialyzed with a CVC until their permanent access was ready to use (we assumed that an AVF could be used after three months and an AVG could be used after 0.5 months). As rates of bacteremia associated with CVCs may vary considerably depending on local practices, these figures may underestimate the benefits of AVFs over AVGs and overestimate those of AVGs over CVCs at some centers.[34,35] The same approach could be used to compare treatment strategies for prevention of sepsis, a less common but more severe complication, as we did above for modality selection, or for prevention of vascular access infections

Table 2 | Number needed to treat with preferred access type to prevent one episode of vascular access–related bacteremia due to non-preferred access

Treatment strategy to prevent bacteremia	65–69 years			70–74 years			75–79 years			80–84 years			85–89 years			⩾90 years		
	Quartiles of life expectancy																	
	75th	50th	25th	75th	50th	25th	75th	50th	25th	75th	50th	25th	75th	50th	25th	75th	50th	25th
AVF vs. AVG Model 1	9	17	48	10	20	62	11	25	82	14	33	110	18	47	167	24	67	219
AVF vs. AVG Model 2	27	—	—	35	—	—	62	—	—	—	—	—	—	—	—	—	—	—
AVG vs. CVC Model 1	<1	1	4	<1	1	5	<1	2	6	1	2	8	1	4	12	2	5	16
AVG vs. CVC Model 3	<1	1	4	<1	2	5	<1	2	7	1	3	9	1	4	15	2	5	21

Abbreviations: AVF, arteriovenous fistula; AVG, arteriovenous graft; CVC, central venous catheter.
'—' indicates life expectancy is shorter than time required to achieve benefit from intervention.
Model 1: Assumes both access types are functional at the start of dialysis.
Model 2: Assumes patients with AVF dialyze via CVC for 3 months while AVF matures and that patients with an AVG dialyze for 0.5 months with a CVC until the AVG is ready for use.
Model 3: Assumes patients with AVG dialyze via CVC for 0.5 months until the AVG is ready for use.

not associated with bacteremia, a more common but less severe complication.

Table 2 demonstrates that for older adults with more limited life expectancy, AVFs confer a very modest reduction in risk of bacteremia compared with AVGs when measured from the time of first use. For example, among patients in the oldest age group with a life expectancy in the 25th percentile, more than 200 AVFs would be needed to prevent one episode of AVG-related bacteremia. For patients with longer life expectancy, the benefits of AVFs vs. AVGs in reducing the risk of bacteremia are more tangible. For example, nine AVFs would be needed to prevent one episode of AVG-related bacteremia in patients aged 65–69 with a life expectancy in the 75th percentile. AVF placement is associated with a relatively greater reduction in risk of bacteremia among patients in the oldest age group with a life expectancy in the 75th percentile than for patients in the youngest age group with a life expectancy in the 25th percentile. Strikingly, any advantages of AVF over AVG placement disappear for most groups when we factor in a relatively modest lag between the access creation and first use. Assuming that an AVF can be used after 3 months and an AVG after 2 weeks, only patients aged 65–80 with a life expectancy in the 75th percentile for their age group would be expected to derive a benefit from AVF vs. AVG placement. These findings suggest that AVFs do not result in a lower lifetime risk of bacteremia compared with AVGs in most older patients without a permanent access at onset of ESRD, and that only those with longer life expectancy will benefit from pre-emptive AVF placement.

As rates of bacteremia are an order of magnitude greater for CVCs compared with AVGs, much less time is required before the risk of bacteremia associated with a CVC exceeds that associated with an AVG. For example, among patients aged 65–69 with a life expectancy in the 75th percentile, less than one AVG would be required to prevent one episode of CVC-related bacteremia. Even among patients in this age group with a life expectancy in the 25th percentile, only four AVGs would be required to prevent one episode of CVC-related bacteremia. Similar to the benefits of AVFs vs. AVGs, the relative benefits of AVGs vs. CVCs decline with age and life expectancy. Due to the shorter lag between access creation and first use for AVGs compared with AVFs, the benefits of AVG vs. CVC use would be predicted to be much less sensitive to timing of AVG placement, although this could vary depending on the timing of AVG placement. One recent study in which AVGs were placed a median of 48 days after dialysis initiation found an increased risk of catheter-related bacteremia compared with pre-dialysis AVG placement.[36]

KIDNEY TRANSPLANTATION

Population-level risks and benefits of kidney transplantation

Decisions to pursue kidney transplantation involve considerations of the risks and benefits of transplantation, and of the transplantation referral and evaluation process. Thus, clinicians need to consider not simply whether transplantation is likely to be beneficial in older adults, but whether a strategy of transplant referral and evaluation is likely to be beneficial. No specific age has been formally defined as an upper limit for transplant candidacy, but rather, guidelines suggest basing candidacy on 'biologic rather than chronologic age'.[37] The criteria for accepting an older adult to the waiting list are highly variable across centers and regions, and this variation may affect the overall assessment of benefit from pursuing transplantation. Living donor transplantation is associated with improved survival compared with deceased donor transplantation in all age groups examined.[38] As patterns of referral, acceptance, and timing of transplantation differ according to whether a living donor is available, here we focus on the risks and benefits of deceased donor kidney transplantation.

The population-level benefits of deceased donor kidney transplantation over chronic dialysis have been well established. Long-term mortality is 48 to 82% lower among deceased-donor transplant recipients than for patients on the waiting list, translating into a doubling of life expectancy for the average transplant recipient.[39] Older adults can also benefit from kidney transplantation. For example, compared with patients who remain on the waiting list, transplantation extends life by 4, 3, and 1 additional year for patients aged 60–64, 65–69, and 70–74, respectively.[39] A more recent

analysis demonstrates that the benefits of transplantation extend to wait-listed patients over the age of 75, and to patients over the age of 70 with diabetes.[40] Jassal and colleagues found that kidney transplantation was cost-effective for patients over the age of 65, but that the attractiveness of transplantation declined as waiting time increased.[41] Short-term allograft survival is slightly lower for older vs. younger adults but still excellent.[40] These benefits should be interpreted in the light of the strong selection bias against older adults during the transplant referral, evaluation and wait-listing process.[42–44]

The benefits of kidney transplantation do not accrue immediately. Rather, transplant recipients incur an upfront risk of mortality for the potential of a long-term benefit. On average, the risk of death during the first 2 weeks after transplantation is almost three-fold higher than that for patients who remain on dialysis.[39] This risk declines over time and by eight months postoperatively, the cumulative mortality from transplantation drops below that of wait-listed patients who remain on dialysis.[39] The length of time it takes for transplantation to yield a survival benefit is longer for older patients, reflecting higher postoperative mortality rates (Figure 3).[39,40]

Beyond postoperative mortality, other potential harms arising from transplantation and the evaluation process should be considered. Although kidney transplantation reduces long-term mortality on average, it increases the risk for certain morbidities, including diabetes, some malignancies and bone fractures. Several types of harm may also arise from the transplant evaluation. First, complications may occur as a result of diagnostic tests or procedures that are part of the transplant evaluation. Second, the evaluation may lead to unnecessary treatment of some conditions (e.g., treatment of low-grade prostate cancer). Third, false-positive test results as a consequence of screening may lead to psychological distress. Fourth, the transplant evaluation process may take time away from other health priorities.

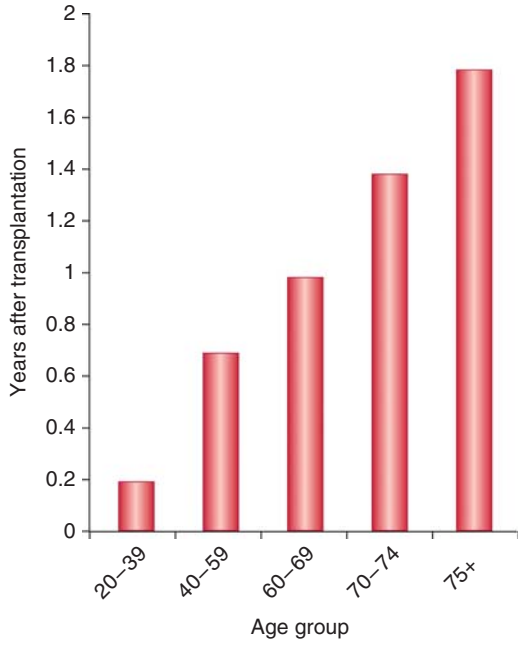

Figure 3 | Time required for cumulative survival after kidney transplantation to exceed cumulative survival on the waiting list, by age group. Data are adapted from Wolfe *et al.*[39] and Rao *et al.*[40]

The advantages of transplantation cannot be realized until patients are placed on the waiting list. For patients over 65 who are ultimately placed on the waiting list, the time from dialysis initiation to wait-listing averages 7-8 months in the US (Supplementary Information online). The longer the evaluation process or the waiting time following dialysis initiation, the higher the rate of death or inactivation due to the development of serious comorbidity. This lowers the net likelihood of benefit from pursuing kidney transplantation.

Risks and benefits of kidney transplantation in patients with different life expectancies

We considered the benefits of deceased donor transplantation vs. remaining on dialysis for patients of different life expectancies. We assumed that patients were active on the waiting list at the start of dialysis, and that transplantation confers a benefit over remaining on the waiting list after 1.0–1.8 years (Supplementary Information online). Table 3 demonstrates that for older patients with a life expectancy below the 25th percentile, deceased-donor transplantation offers no additional benefit compared with remaining on dialysis. However, the benefits of transplantation are fairly robust for older patients with a life expectancy above the 75th percentile. For example, four transplants would be needed to prevent one death on the waiting list for patients aged 65–69 with a life expectancy above the 75th percentile. As would be anticipated, the benefit of transplantation declines with age. Still, for patients up to 84 years of age in the highest quartile of life expectancy, the NNT to prevent one death on the waiting list appears low enough to justify transplantation, assuming patients are active on the waiting list at the start of dialysis. When the lag time to wait-listing is factored in, the benefits of transplantation are lower. This is most clearly demonstrated for patients in the 70–74-year age group with a life expectancy near the median, where the NNT increases from 19 to 402 with the incorporation of a 7-month delay from the start of dialysis to wait-listing. For patients aged 65–79 with a life expectancy above the 75th percentile, transplantation remains favorable even after accounting for a delay in wait-listing.

These estimates may be modified by patient or regional factors. For example, if 10% of waiting time is spent in inactive status,[40] then the NNT remains below 10 only for patients aged 65–74 with a life expectancy above the 75th percentile. Very long waiting times may also affect the relative advantages of an expanded criteria donor (ECD) vs. a standard criteria donor (SCD). The ECD list shortens waiting times compared with the SCD list, but at the expense of a higher risk for allograft loss. Patients more vulnerable to

Table 3 | Number needed to transplant to prevent one death on waiting list

	65–69 years			70–74 years			75–79 years			80–84 years			85–89 years			⩾90 years		
	Quartiles of life expectancy																	
Treatment strategy	75th	50th	25th	75th	50th	25th	75th	50th	25th	75th	50th	25th	75th	50th	25th	75th	50th	25th
Deceased donor txp vs. waitlist Model 1	4	9	—	5	19	—	7	—	—	11	—	—	25	—	—	—	—	—
Deceased donor txp vs. waitlist Model 2	4	17	—	6	402	—	10	—	—	21	—	—	—	—	—	—	—	—

Abbreviation: txp, transplant.
'—' indicates life expectancy is shorter than time required to achieve benefit from intervention.
Model 1: Assumes patients are active on waiting list at the start of dialysis.
Model 2: Incorporates age-specific lag from start of dialysis to transplant wait-listing (Supplementary Information online).

poorer health or death while on the waitlist, and those in regions with longer waiting times may benefit from an ECD transplant.[45] For example, in regions where the median waiting time exceeds 4 years, the waiting time for an SCD transplant would exceed the life expectancy of most patients over the age of 65. In contrast, in regions where the median waiting time is less than 2 years, the choice between ECD and SCD transplantation must be based on the balance between the additional time on the waiting list for an SCD transplant vs. reduced allograft life of an ECD transplant.

Still, determining which older adults will benefit from *initiating* a transplant evaluation and when to begin this process can be challenging. Preemptive transplantation is associated with the largest survival advantage, even in older adults, and as illustrated in Table 3, a delay in placing otherwise suitable patients on the waiting list could reduce the benefits of pursuing transplantation. However, in some cases it may be unclear whether an older patient is likely to progress to ESRD. Initiating a transplant evaluation in these patients would expose them to the potential harms of unnecessary diagnostic testing with little possibility for benefit. Among older patients already on dialysis, there may be uncertainty about the outcome of the transplant evaluation. Thus, there may also be reluctance to refer patients for transplantation if the likelihood of successfully completing the transplant workup is felt to be low. In one study 27% of patients over age 55 and interested in transplantation completed the transplant evaluation and were placed on the waiting list.[46] If applied to the data in Table 3, then 15 patients aged 65–69 with a life expectancy above the 75th percentile and 63 patients with a life expectancy near the median would need to be referred, respectively, in order to prevent one death on dialysis. These data illustrate how non-transparent wait-listing practices may make initiation of a transplant evaluation an unattractive management strategy among otherwise suitable candidates.

PATIENT PREFERENCES

The last step in this framework is the incorporation of patient preferences. It allows for the possibility that different patients may require very different benefit thresholds (i.e., NNTs) to favor a given treatment strategy and may prioritize outcomes differently. In other words, the outcomes that matter most to clinicians and policy-makers may not be the ones that matter most to patients. For example, the decision to place an AVG over a CVC in an 85-year-old patient with poor life expectancy may not be considered straightforward (NNT 15 to prevent one episode of CVC-related bacteremia). By incorporating the patient's preferences, such as a desire to avoid cannulation pain and focus on short-term goals, the appropriate course may become more apparent. In one study 30% of patients were willing to accept a substantially higher mortality risk in order to remain on their current modality.[20] Similar findings are suggested in qualitative studies of vascular access preferences.[47] The decision to pursue kidney transplantation in a 65-year-old patient with above average life expectancy may seem clear-cut (NNT 4-17). However, for patients with concerns about the postoperative risks or a desire to avoid the uncertainties of the evaluation process, it may not be worth the potential benefits. For this framework to be effective, it is imperative that information is communicated when patients are receptive, that misperceptions are clarified, and that modifiable barriers to care are addressed. Clinicians should also be mindful that preferences evolve over time and may need to be revisited.[48]

COMMENT

We have outlined a framework for individualizing renal replacement therapy decisions in older patients. The advantage of this framework is that it provides a systematic approach to consider risks, benefits and preferences for competing treatment strategies based on life expectancy. In doing so, it highlights how ESRD care might be optimized for the subset of patients with the lowest life expectancy and highest costs of care, a group often neglected in clinical trials or practice guidelines. The specific quantitative estimates of benefits and risks that we use to illustrate this approach are limited by the availability of comparative-effectiveness data and the lack of randomized controlled trials for many management decisions in ESRD. Unmeasured selection biases may have caused us to overestimate the benefits of certain treatment strategies, although these same limitations also apply to widely used practice guidelines. In addition, uncertainty about whether and when older adults will initiate

chronic dialysis may impact decisions about preparatory interventions such as pre-emptive access placement and transplant. This framework can be updated as new information becomes available and could be applied to other aspects of ESRD care. In several instances, this approach might provide support for treatment decisions that directly contradict available practice guidelines, illustrating circumstances when strict application of guidelines may be inappropriate for certain patients. In summary, by identifying effective treatments that align with patient priorities, this framework may be able to improve the overall quality of ESRD care for older patients.

DISCLOSURE

All the authors declared no competing interests.

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SUPPLEMENTARY MATERIAL

Appendix Table 1. Incidence rate of sepsis hospitalization and modality transfer rates.

Appendix Table 2. Incidence of access-related bacteremia according to vascular access type.

Appendix Table 3. Median time to placement on the transplant waiting list, time to equal cumulative mortality after transplant, and incidence of death after equal cumulative mortality.

Supplementary material is linked to the online version of the paper at http://www.nature.com/ki

REFERENCES

1. O'Hare AM, Rodriguez RA, Hailpern SM *et al.* Regional variation in health care intensity and treatment practices for end-stage renal disease in older adults. *JAMA* 2010; **304**: 180–186.
2. Kurella M, Covinsky KE, Collins AJ *et al.* Octogenarians and nonagenarians starting dialysis in the United States. *Ann Intern Med* 2007; **146**: 177–183.
3. Boyd CM, Darer J, Boult C *et al.* Clinical practice guidelines and quality of care for older patients with multiple comorbid diseases: implications for pay for performance. *JAMA* 2005; **294**: 716–724.
4. Walter LC, Covinsky KE. Cancer screening in elderly patients: a framework for individualized decision making. *JAMA* 2001; **285**: 2750–2756.
5. Bogardus Jr ST, Holmboe E, Jekel JF. Perils, pitfalls, and possibilities in talking about medical risk. *JAMA* 1999; **281**: 1037–1041.
6. Moss AH, Ganjoo J, Sharma S *et al.* Utility of the 'surprise' question to identify dialysis patients with high mortality. *Clin J Am Soc Nephrol* 2008; **3**: 1379–1384.
7. Miskulin DC, Martin AA, Brown R *et al.* Predicting 1 year mortality in an outpatient haemodialysis population: a comparison of comorbidity instruments. *Nephrol Dial Transplant* 2004; **19**: 413–420.
8. Cohen LM, Ruthazer R, Moss AH *et al.* Predicting six-month mortality for patients who are on maintenance hemodialysis. *Clin J Am Soc Nephrol* 2010; **5**: 72–79.
9. Couchoud C, Labeeuw M, Moranne O *et al.* A clinical score to predict 6-month prognosis in elderly patients starting dialysis for end-stage renal disease. *Nephrol Dial Transplant* 2009; **24**: 1553–1561.
10. Geddes CC, van Dijk PC, McArthur S *et al.* The ERA-EDTA cohort study—comparison of methods to predict survival on renal replacement therapy. *Nephrol Dial Transplant* 2006; **21**: 945–956.
11. Mehrotra R, Chiu YW, Kalantar-Zadeh K *et al.* Similar outcomes with hemodialysis and peritoneal dialysis in patients with end-stage renal disease. *Arch Intern Med* 2011; **171**: 110–118.
12. Weinhandl ED, Foley RN, Gilbertson DT *et al.* Propensity-matched mortality comparison of incident hemodialysis and peritoneal dialysis patients. *J Am Soc Nephrol* 2010; **21**: 499–506.
13. Jaar BG, Plantinga LC, Crews DC *et al.* Timing, causes, predictors and prognosis of switching from peritoneal dialysis to hemodialysis: a prospective study. *BMC Nephrol* 2009; **10**: 3.
14. Lim W, Dogra G, McDonald SP *et al.* Compared with younger peritoneal dialysis patients, elderly patients have similar peritonitis-free survival and lower risk of technique failure, but higher risk of peritonitis-related mortality. *Perit Dial Int* 2011 (e-pub ahead of print).
15. Wu AW, Fink NE, Marsh-Manzi JV *et al.* Changes in quality of life during hemodialysis and peritoneal dialysis treatment: generic and disease specific measures. *J Am Soc Nephrol* 2004; **15**: 743–753.
16. Shih YC, Guo A, Just PM *et al.* Impact of initial dialysis modality and modality switches on Medicare expenditures of end-stage renal disease patients. *Kidney Int* 2005; **68**: 319–329.
17. Collins AJ, Foley RN, Herzog C *et al.* Excerpts from the US renal data system 2009 annual data report. *Am J Kidney Dis* 2010; **55**: S1–420, A426–427.
18. Jaar BG, Coresh J, Plantinga LC *et al.* Comparing the risk for death with peritoneal dialysis and hemodialysis in a national cohort of patients with chronic kidney disease. *Ann Intern Med* 2005; **143**: 174–183.
19. Perl J, Wald R, McFarlane P *et al.* Hemodialysis vascular access modifies the association between dialysis modality and survival. *J Am Soc Nephrol* 2011; **22**: 1113–1121.
20. Bass EB, Wills S, Fink NE *et al.* How strong are patients' preferences in choices between dialysis modalities and doses? *Am J Kidney Dis* 2004; **44**: 695–705.
21. Oliver MJ, Verrelli M, Zacharias JM *et al.* Choosing peritoneal dialysis reduces the risk of invasive access interventions. *Nephrol Dial Transplant* 2011 (e-pub ahead of print).
22. Vascular Access Work Group. Clinical practice guidelines for vascular access. *Am J Kidney Dis* 2006; **48**(Suppl 1): S248–S273.
23. Peterson WJ, Barker J, Allon M. Disparities in fistula maturation persist despite preoperative vascular mapping. *Clin J Am Soc Nephrol* 2008; **3**: 437–441.
24. Levine MI. A challenge for nephrologists—increasing fistula maturation rates, reducing fistula maturation time, and decreasing dialysis catheter prevalence in the United States. *Semin Dial* 2008; **21**: 280–284.
25. Foley RN, Chen SC, Collins AJ. Hemodialysis access at initiation in the United States, 2005 to 2007: still 'catheter first'. *Hemodial Int* 2009; **13**: 533–542.
26. Xue H, Lacson Jr E, Wang W *et al.* Choice of vascular access among incident hemodialysis patients: a decision and cost-utility analysis. *Clin J Am Soc Nephrol* 2010; **5**: 2289–2296.
27. Ravani P, Parfrey P, MacRae J *et al.* Modeling survival of arteriovenous accesses for hemodialysis: semiparametric versus parametric methods. *Clin J Am Soc Nephrol* 2010; **5**: 1243–1248.
28. Allon M, Lok CE. Dialysis fistula or graft: the role for randomized clinical trials. *Clin J Am Soc Nephrol* 2010; **5**: 2348–2354.
29. O'Hare AM, Allon M, Kaufman JS. Whether and when to refer patients for predialysis AV fistula creation: complex decision making in the face of uncertainty. *Semin Dial* 2010; **23**: 452–455.
30. O'Hare AM, Bertenthal D, Walter LC *et al.* When to refer patients with chronic kidney disease for vascular access surgery: should age be a consideration? *Kidney Int* 2007; **71**: 555–561.
31. Kaufman SR, Shim JK, Russ AJ. Old age, life extension, and the character of medical choice. *J Gerontol B Psychol Sci Soc Sci* 2006; **61**: S175–S184.
32. Richardson II AI, Leake A, Schmieder GC *et al.* Should fistulas really be first in the elderly patient? *J Vasc Access* 2009; **10**: 199–202.
33. Klevens RM, Edwards JR, Andrus ML *et al.* Dialysis Surveillance Report: National Healthcare Safety Network (NHSN)-data summary for 2006. *Semin Dial* 2008; **21**: 24–28.
34. James MT, Manns BJ, Hemmelgarn BR *et al.* What's next after fistula first: is an arteriovenous graft or central venous catheter preferable when an arteriovenous fistula is not possible? *Semin Dial* 2009; **22**: 539–544.
35. Power A, Singh SK, Ashby D *et al.* Long-term Tesio catheter access for hemodialysis can deliver high dialysis adequacy with low complication rates. *J Vasc Interv Radiol* 2011; **22**: 631–637.
36. Shingarev R, Maya ID, Barker-Finkel J *et al.* Arteriovenous graft placement in predialysis patients: a potential catheter-sparing strategy. *Am J Kidney Dis* 2011; **58**: 243–247.
37. Danovitch G, Savransky E. Challenges in the counseling and management of older kidney transplant candidates. *Am J Kidney Dis* 2006; **47**: S86–S97.
38. Cooper M, Forland CL. The elderly as recipients of living donor kidneys, how old is too old? *Curr Opin Organ Transplant* 2011; **16**: 250–255.
39. Wolfe RA, Ashby VB, Milford EL *et al.* Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and

recipients of a first cadaveric transplant. *N Engl J Med* 1999; **341**: 1725–1730.
40. Rao PS, Merion RM, Ashby VB *et al.* Renal transplantation in elderly patients older than 70 years of age: results from the Scientific Registry of Transplant Recipients. *Transplantation* 2007; **83**: 1069–1074.
41. Jassal SV, Krahn MD, Naglie G *et al.* Kidney transplantation in the elderly: a decision analysis. *J Am Soc Nephrol* 2003; **14**: 187–196.
42. Kiberd B, Boudreault J, Bhan V *et al.* Access to the kidney transplant wait list. *Am J Transplant* 2006; **6**: 2714–2720.
43. Schold J, Srinivas TR, Sehgal AR *et al.* Half of kidney transplant candidates who are older than 60 years now placed on the waiting list will die before receiving a deceased-donor transplant. *Clin J Am Soc Nephrol* 2009; **4**: 1239–1245.
44. Schaeffner ES, Rose C, Gill JS. Access to kidney transplantation among the elderly in the United States: a glass half full, not half empty. *Clin J Am Soc Nephrol* 2010; **5**: 2109–2114.
45. Merion RM, Ashby VB, Wolfe RA *et al.* Deceased-donor characteristics and the survival benefit of kidney transplantation. *JAMA* 2005; **294**: 2726–2733.
46. Alexander GC, Sehgal AR. Barriers to cadaveric renal transplantation among blacks, women, and the poor. *JAMA* 1998; **280**: 1148–1152.
47. Xi W, Harwood L, Diamant MJ *et al.* Patient attitudes towards the arteriovenous fistula: a qualitative study on vascular access decision making. *Nephrol Dial Transplant* 2011; **26**: 3302–3308.
48. Fried TR, Van Ness PH, Byers AL *et al.* Changes in preferences for life-sustaining treatment among older persons with advanced illness. *J Gen Intern Med* 2007; **22**: 495–501.